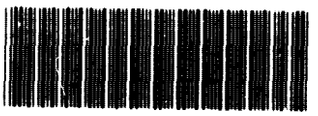
8EHQ-92-8005
INIT

UNION CARBIDE CHEMICALS AND PLASTICS COMPANY INC.

HEALTH, SAFETY AND ENVIRONMENTAL AFFAIRS 8EHQ-0892-8005

August 21, 1992

CERTIFIED MAIL
RETURN RECEIPT REQUESTED



88920006651

Document Processing Center (TS-790)
Room L-100
Office of Toxic Substances
U.S. Environmental Protection Agency
401 M Street, SW
Washington, DC 20460

Attn: Section 8(e) Coordinator (CAP Agreement)

Re: CAP Agreement Identification No. 8ECAP-0110

Dear Sir or Madam:

Union Carbide Corporation ("Union Carbide") herewith submits the following report pursuant to the terms of the TSCA §8(e) Compliance Audit Program and Union Carbide's CAP Agreement dated August 14, 1991 (8ECAP-0110). This report describes a vapor inhalation study with isophorone (CASRN 78-59-1).

"Summary of Response of Guinea Pigs and Rats to Repeated Inhalation of the Vapors of Isophorone", Mellon Institute of Industrial Research (University of Pittsburgh), Report 4-59b, July 8, 1941.

A complete summary of this report is attached.

Previous TSCA Section 8(e) or "FYI" Submission(s) related to this substance are:

(None)

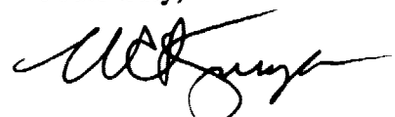
Previous PMN submissions related to this substance are: (None)

4-59b

This information is submitted in light of EPA's current guidance. Union Carbide does not necessarily agree that this information reasonably supports the conclusion that the subject chemical presents a substantial risk of injury to health or the environment.

In the attached report the term "CONFIDENTIAL" may appear. This precautionary statement was for internal use at the time of issuance of the report. Confidentiality is hereby waived for purposes of the needs of the Agency in assessing health and safety information. The Agency is advised, however, that the publication rights to the contained information are the property of Union Carbide.

Yours truly,



William C. Kuryla, Ph.D.
Associate Director
Product Safety
(203/794-5230)

WCK/cr
Attachment (3 copies of cover letter, summary, and report)

SUMMARY

Confidential

(Report 4-59b)

R: 7-8-41

O.K. E.G.T.

MELLON INSTITUTE OF INDUSTRIAL RESEARCH

UNIVERSITY OF PITTSBURGH

SPECIAL REPORT

on

SUMMARY OF RESPONSE OF GUINEA PIGS AND RATS TO

REPEATED INHALATION OF THE VAPORS OF ISOPHORONE

Carbide and Carbon Chemicals Corporation Industrial Fellowship No. 274-4

On 4-11-40 a report was issued presenting the results of single exposures to these vapors. In that report it was shown that 750 p.p.m. is the maximum concentration to which rats and guinea pigs may be exposed for several hours with slight or no symptoms. When death occurred it was usually during an exposure, due to paralysis of the respiratory center. The few delayed deaths were due to lung irritation. Microscopic pathology of survivors was never severe, and centered in the lung, kidney, heart, liver, and spleen with frequency in that order.

The present report summarizes the results of exposing animals 8 hours a day for 30 days to Isophorone vapors.

Kidneys were much more frequently injured, with necrosis of tubular epithelium the worst effect, noted only in one rat inhaling 500 p.p.m., and cloudy swelling with increased secretion and dilation of Bowman's capsule a common finding.

XVII

Confidential

R: 7-8-41

(Report 4-59b)

O.K. E.G.T.

MELLON INSTITUTE OF INDUSTRIAL RESEARCH

UNIVERSITY OF PITTSBURGH

SPECIAL REPORT

on

SUMMARY OF RESPONSE OF GUINEA PIGS AND RATS TO

REPEATED INHALATION OF THE VAPORS OF ISOPHORONE

Carbide and Carbon Chemicals Corporation Industrial Fellowship No. 274-4

On 4-11-40 a report was issued presenting the results of single exposures to these vapors. In that report it was shown that 750 p.p.m. is the maximum concentration to which rats and guinea pigs may be exposed for several hours with slight or no symptoms. When death occurred it was usually during an exposure, due to paralysis of the respiratory center. The few delayed deaths were due to lung irritation. Microscopic pathology of survivors was never severe, and centered in the lung, kidney, heart, liver; and spleen with frequency in that order.

The present report summarizes the results of exposing animals 8 hours a day for 30 days to Isophorone vapors.

Methods were similar to those of the previous study. A commercial sample was used.

Animals were observed for about two weeks before use, selecting those growing normally for exposure. Usually 10 white rats and 10 guinea pigs were selected for a series, and exposed 8 hours a day 5 days a week for six weeks. Weights were followed, blood counts were made frequently on some of the animals, urines were examined, and tissues were studied at the end of the exposure period. Concentrations of 500, 200, 100, 50, and 25 p.p.m. were used.

Results are summarized in Table 4-104, below.

Table 4-104

Summary of Effects from Repeated Exposures to Isophorone Vapors

Species	P.P.M.	Nose and Eye Irritation	Wt. Loss	Blood Cell Changes	Urine Albumin	Urine Sugar(1)	Pathology (2)	Death (3)
Rats	500	+	0	0	+	?	33 %	50 %
	200	0	0	0	0	?	75	10
	100	0	0	0	0	?	80	20
	50	0	0	0	0	?	67	0
	25	0	0	0	0	?	0	0
Guinea Pigs	500	+	+	+	0	?	83	40
	200	0	+	0	0	?	33	25
	100	0	+	0	0	?	67	0
	25	0	0	0	0	0	0	0

(1) ? means reducing substance present, probably not sugar
(2) % of survivors examined having pathology in liver or kidney
(3) % of animals dying of toxic action

In these animals repeated exposure to an excess of isophorone vapors was found to produce:-

conjunctivitis and nasal irritation	at 500 p.p.m.
urinary albumin	at 500 p.p.m.
increase in polymorphonuclear white cells	at 500 p.p.m.
occasional light cloudy swelling in liver	at 50 p.p.m.
necrosis in kidney	at 500 p.p.m.
cloudy swelling in kidney	at 50 p.p.m.
lung irritation	at 50 p.p.m.
death	at 100 p.p.m.

Small animals should not inhale more than 25 p.p.m. of isophorone vapors repeatedly for long periods of time. Presumably human exposure should also be kept below this level.

Henry F. Smyth, Jr.

Henry F. Smyth, Jr.

SENIOR INDUSTRIAL FELLOW

July 10, 1941-abc

MELLON INSTITUTE OF INDUSTRIAL RESEARCH

UNIVERSITY OF PITTSBURGH

SPECIAL REPORT

on

Response of Guinea Pigs and Rats to

Repeated Inhalation of the Vapors of Isophorone

Carbide & Carbon Chemicals Corporation Industrial Fellowship No. 274-4

TABLE OF CONTENTS

On 4-11-40 a report was issued presenting the results of single exposures to these vapors. In that report it was shown that 750 p.p.m. is the maximum concentration to which rats and guinea pigs may be exposed for several hours with slight or no symptoms. When death occurred it was usually during an exposure, due to paralysis of the respiratory center. The few delayed deaths were due to lung irritation. Microscopic pathology of survivors was never severe, and centered in the lung, kidney, heart, liver, and spleen, with frequency in that order.

The present report describes the results of exposing animals 8 hours a day for 30 days to isophorone vapors.

Methods

Methods were similar to those of the previous study. A commercial sample was used. The vapor concentrations were maintained by bubbling air through the solvent in a constant temperature bath, and diluting this vapor stream with pure air. The resulting mixture was checked by an interferometer frequently. This instrument was not sensitive enough to check 25 and 50 p.p.m. concentrations, so activated charcoal adsorption was resorted to for selecting flowmeter settings.

Animals were observed for about two weeks before use, selecting those growing normally for exposure. Usually 10 white rats and 10 guinea pigs were selected for a series and exposed 8 hours a day 5 days a week for six weeks. Weights were followed, blood counts were made frequently on some of the animals, urines were examined, and tissues were studied at the end of the exposure period. Concentrations of 500, 200, 100, 50, and 25 p.p.m. were used.

The original plan was to kill some animals after 10, some after 20, and the rest after 30 exposures. Accidents and infections interfered with this, and it was found better toward the end of the work to continue all animals for 30 exposures.

Results

Results are summarized in Table 4-104 below, and discussed by type of action following this, with more detailed tables later in this report.

Table 4-104

Summary of Effects from Repeated Exposures to Isophorone Vapors

Species	P.P.M.	Nose and Eye Irritation	Weight Loss	Blood Cell Changes	Urine Albumin	Urine Sugar (1)	Pathology (2)	Death (3)
Rats	500	+	0	0	+	?	33%	50%
	200	0	0	0	0	?	75	10
	100	0	0	0	0	?	80	20
	50	0	0	0	0	?	67	0
	25	0	0	0	0	?	0	0
Guinea pigs	500	+	+	+	0	?	83	40
	200	0	+	0	0	?	33	25
	100	0	+	0	0	?	67	0
	25	0	0	0	0	0	0	0

(1) ? means reducing substance present, probably not sugar
(2) % of survivors examined having pathology in liver or kidney
(3) % of animals dying of toxic action

Death

About half the animals exposed to 500 p.p.m. isophorone vapors eight hours a day died from the effects before the thirtieth exposure. No guinea pigs died from 100 p.p.m. or less and no rats from 50 p.p.m. or less.

Death appeared to be due to a combination of actions upon kidney and lung. Sometimes the one organ was more severely injured, sometimes the other.

Infection

During part of the study we had much trouble with infections, the guinea pigs being particularly bad. Control animals and exposed animals alike were affected. These consisted of a variety of agents, parasites, intestinal protozoa, and bacteria.

Many deaths were obviously due to these infections, and these animals have been eliminated from consideration even though it is possible that the exposures contributed to the deaths.

Irritation

No corneal necrosis resulted even from 30 eight-hour exposures to 500 p.p.m. of isophorone vapors. At this concentration chronic conjunctivitis and nasal irritation developed in both rats and guinea pigs, but neither were evident at 200 p.p.m. or less.

Diarrhea

No diarrhea developed from any concentration, although this was a symptom of action previously found in single exposures to higher concentrations. Small animals are not very sensitive indicators for low grade intestinal irritation, so it is possible that humans inhaling 200 or 500 p.p.m. of isophorone for several hours day after day might experience increased peristalsis or even frank diarrhea.

Growth

No consistent effect of any of these repeated exposures upon growth of survivors was seen, although the animals were young and still growing actively, hence quite susceptible to any injurious agencies. Details appear in Table 4-107 at the end of this report.

Victims of the exposures lost weight before death, and were generally weak with poor appetite.

Urine

Urine from animals exposed to 500 p.p.m. was examined five times, and from other animals less frequently. Only those inhaling 500 p.p.m. produced any albumin in spite of the definite kidney injury found in other animals by microscopic examination.

On the face of the sugar results, one might claim that isophorone injured liver and kidney sufficiently to cause poor sugar utilization or excessive excretion. We do not believe this to be the case, for liver showed insufficient pathology to explain poor utilization and urinary albumin was rare. It seems more likely that the reducing substance reported as sugar was some elimination product of isophorone.

A summary of urine findings appears in Table 4-105 below.

Table 4-105

Summary of Urine Examinations

(Pooled Urine From Group)

Species	P.P.M.	Times Examined	Albumin	Sugar %	Control Sugar %
Rats	500	5	Trace	1.5	0.83
	200	3	0	1.2	0.77
	100	4	0	0.7	0.55
	50	3	0	0.9	0.78
	25	1	0	0.8	0.69
Guinea pigs	500	5	0	2.6	1.6
	200	5	0	1.1	0.7
	100	4	0	0.72	0.6
	25	1	0	0.70	0.7

Blood Count

Blood counts were made repeatedly on the animals and the results appear in Table 4-108 at the end of this report. Guinea pigs exposed to 500 p.p.m. showed a significant increase in polymorphonuclear white cells and a corresponding fall in lymphocytes. Otherwise no consistent change in blood counts was found.

Gross Pathology

Grossly upon autopsy, bile was red or orange, kidney pale or brownish, liver pale, spleen congested, and lung congested or hemorrhagic. These findings were usually confirmed upon microscopic examination, although there was insufficient liver pathology to explain the frequent indications of excess bile pigment.

Microscopic Pathology

Details of microscopic pathology appear in Table 4-109 at the end of this report, and Table 4-106 below presents a summary.

Table 4-106

Summary of Pathology in Surviving Uninfected Animals

(See Abbreviation Key After Table 4-109)

Species	P.P.M.	Organ	Number Examined	No. with Pathology	Worst Pathology	Other Pathology
Rat	500	Kidney	3	1	Knt	-
		Liver	2	0	-	-
		Lung	2	1	LUc	-
		Spleen	3	1	Sc	-
	200	Kidney	4	3	Kcntw	Ks
		Liver	3	0	-	-
		Lung	4	4	LUcr	LUc, LUr
		Spleen	4	2	Sc	-
	100	Kidney	5	4	Kctw	Ktw
		Liver	5	0	-	-
		Lung	5	5	LUcs	LUc, LUcr
		Spleen	5	4	Sc	-
	50	Kidney	6	4	Kw	Kg, Kb, Kt
		Liver	6	1	Lw	-
		Lung	6	5	LUces	LUc, LUs, LUcs
		Spleen	6	0	-	-
	25	Kidney	5	0	-	-
		Liver	5	0	-	-
		Lung	5	6	LUc	-
		Spleen	0	-	-	-

(Continued)

Table 4-106 Cont'd

Species	P.P.M.	Organ	Number Examined	No. with Pathology	Worst Pathology	Other Pathology
Guinea pig	500	Kidney	6	5	Kbdsw	Kw, Kbcsw
		Liver	6	1	Lw	-
		Lung	5	5	LUCfrs	LUc, LUcs, LUCrs
		Spleen	6	0	-	-
	200	Kidney	3	1	Kw	-
		Liver	3	0	-	-
		Lung	3	3	LUber	LUc, LUac
		Spleen	3	0	-	-
	100	Kidney	3	2	Kw	-
		Liver	2	0	-	-
		Lung	2	2	LUcep	LUcrs
		Spleen	3	-	-	-
	25	Kidney	5	0	-	-
		Liver	5	0	-	-
		Lung	5	5	LUc	-
		Spleen	0	-	-	-

The heart muscle was uniformly normal, and the spleen was never affected more severely than congestion. No deposits of pigment in the spleen indicated red blood cell destruction.

Of 37 livers examined, only two showed any pathology, each having slight cloudy swelling. Thus, action of small amounts of isophorone on the liver is negligible.

Kidneys were much more frequently injured, with necrosis of tubular epithelium the worst effect, noted only in one rat inhaling 500 p.p.m., and cloudy swelling with increased secretion and dilation of Bowman's capsule a common finding.

Lungs were also frequently injured. This injury consisted of congestion and leakage of red cells into alveoli chiefly. Gross hemorrhage has been attributed to trauma during sacrifice by severing spinal cord, not to the exposure. The whole lung picture is subject to some discount due to our past experience, where we found

rat and guinea pig lungs much more susceptible to irritation from vapors than are human lungs.

Concentration vs. Effect

No effect whatever was seen from 25 p.p.m. eight hours a day for 30 days. Fifty p.p.m. and higher concentrations produced increasing effect as the concentration rose. One hundred p.p.m. caused some deaths.

Summary of Effects Noted

In small animals repeated exposure to an excess of isophorone vapors was found to produce:

Conjunctivitis and nasal irritation.	at 500 p.p.m.
Urinary albumin.	at 500 p.p.m.
Increase in polymorphonuclear white cells.	at 500 p.p.m.
Occasional light cloudy swelling in liver.	at 50 p.p.m.
Necrosis in kidney	at 500 p.p.m.
Cloudy swelling in kidney.	at 50 p.p.m.
Lung irritation.	at 50 p.p.m.
Death.	at 100 p.p.m.

Conclusions

Small animals should not inhale more than 25 p.p.m. of isophorone vapors repeatedly for long periods of time. Presumably human exposure should also be kept below this level.

Henry F. Smyth, Jr.

Henry F. Smyth, Jr.
SENIOR INDUSTRIAL FELLOW

July 10, 1941-mah

Table 4-107

Growth of Animals Surviving Repeated Isophorone Vapor Exposures

P.P.M.	First Exposure	Animal No.	8-hour Exposures	Wt. in Grams	Weight Change During First 10 Exp.	Second 10 Exp.	Third 10 Exp.	30 Exp.
500	10-10-38	R 2739	10	108	+ 48	-	-	-
		R 2737	20	110	+ 27	+ 24	-	-
		R 2738	20	125	+ 15	+ 24	-	-
		R 2733	24	114	+ 39	- 14	-	-
		R 2731	30	124	+ 33	+ 15	+ 54	+102
		Ave.			+ 32	+ 15	+ 54	+102
500	10-10-38	P 3412	10	246	+ 3	-	-	-
		P 3408	20	246	- 18	+ 17	-	-
		P 3409	20	246	- 36	- 2	-	-
		P 3404	30	218	- 4	+ 10	+ 36	+ 42
		P 3406	30	244	- 6	+ 10	+ 36	+ 40
		P 3407	30	268	- 30	+ 17	+ 19	+ 6
		Ave.			- 13.5	+ 10.4	+ 30.3	+ 29.3
200	11-2-38	R 2937	10	137	+ 29	-	-	-
		R 2933	30	119	+ 30	+ 34	+ 12	+ 76
		R 2934	30	108	+ 27	+ 47	+ 24	+ 91
		R 2935	30	118	+ 24	+ 53	+ 16	+ 93
		R 2936	30	100	+ 17	+ 23	+ 23	+ 63
		R 2938	30	103	+ 44	+ 50	+ 29	+123
		R 2939	30	131	+ 39	+ 48	+ 13	+100
		R 2941	30	98	+ 33	+ 35	+ 27	+ 95
		R 2942	30	93	+ 37	+ 30	+ 13	+ 80
		Ave.			+ 31	+ 39	+ 19	+ 90
200	11-28-38	P 3837	10	242	- 51	-	-	-
		P 3838	10	218	- 6	-	-	-
		P 3833	20	270	- 10	- 22	-	-
		P 3835	20	224	+ 28	+ 16	-	-
		P 3742	30	262	- 11	+ 9	+ 91	+ 89
		P 3745	30	250	+ 35	- 25	+ 67	+ 77
		Ave.			- 2.5	+ 5.5	+ 79	+ 83
100	12-1-38	R 3176	20	132	+ 17	+ 35	-	-
		R 3177	20	144	+ 32	+ 22	-	-
		R 3172	30	140	+ 52	+ 44	+ 22	+118
		R 3173	30	121	+ 27	+ 40	+ 22	+ 89
		R 3174	30	133	+ 64	+ 30	+ 19	+113
		R 3175	30	130	+ 36	+ 32	+ 16	+ 84
		R 3178	30	158	+ 51	+ 40	+ 20	+111
		R 3179	30	148	+ 41	+ 44	+ 27	+112
		Ave.			+ 40	+ 36	+ 21	+104

(Continued)

Table 4-107 Cont'd

P.P.M.	First Exposure	Animal No.	8-hour Exposures	Wt. in Grams	Weight Change During First 10 Exp.	Second 10 Exp.	Third 10 Exp.	30 Exp.
100	12-1-38	P 3842	10	253	- 13	-	-	-
		P 3843	10	268	+ 27	-	-	-
		P 3840	20	247	+ 26	- 25	-	-
		P 3841	20	283	+ 37	+110	-	-
		P 3829	30	237	+ 15	+ 14	+ 62	+ 91
		P 3830	30	236	+ 12	+ 1	- 82	- 49
		P 3832	30	219	+ 1	+ 6	- 17	- 10
		Ave.			+ 15	+ 19.2	- 12.3	+ 10.7
50	1-30-39	R 3644	10	121	+ 45	-	-	-
		R 3802	10	118	+ 50	-	-	-
		R 3801	20	131	+ 38	+ 2	-	-
		R 3798	20	119	+ 28	+ 11	-	-
		R 3799	20	114	+ 1	+ 21	-	-
		R 3640	30	114	+ 47	+ 40	+ 22	+109
		R 3641	30	113	+ 52	+ 46	+ 9	+107
		R 3642	30	113	+ 12	+ 37	+ 33	+ 92
		Ave.			+ 34	+ 26	+ 21	+103
25	8-20-40	R 8733	30	120	+ 41	+ 7	+ 41	+ 89
		R 8734	30	141	+ 34	+ 7	+ 42	+ 83
		R 8735	30	125	+ 47	+ 9	+ 59	+115
		R 8737	30	105	+ 40	+ 20	+ 48	+108
		R 8738	30	135	+ 16	- 16	+ 33	+ 33
		R 8739	30	124	+ 42	0	+ 34	+ 76
		R 8740	30	103	+ 33	+ 5	+ 30	+ 68
		R 8741	30	130	+ 16	+ 16	+ 40	+ 72
		R 8747	30	112	+ 30	- 4	+ 26	+ 53
		R 8748	30	113	+ 31	+ 8	+ 62	+ 101
		Ave.			+ 33	+ 5	+ 42	+ 80
25	8-20-40	P 8754	30	272	+ 48	+ 37	- 33	+ 53
		P 8755	30	300	+ 56	- 23	- 3	+ 30
		P 8757	30	241	+ 67	- 19	+ 34	+ 82
		P 8759	30	297	+ 95	+ 18	+ 26	+139
		P 8761	30	289	+ 87	+ 5	+ 81	+173
		P 8763	30	275	+ 62	+ 15	+ 18	+ 95
		P 8769	30	275	+ 75	+ 32	- 6	+101
		P 8770	30	288	+ 84	+ 32	+ 41	+157
		P 8771	30	287	+ 93	- 80	+ 26	+ 39
		P 8772	30	278	+ 43	+ 9	+ 44	+ 96
		Ave.			+ 71	+ 2	+ 23	+ 96

(Continued)

Table 4-107 Cont'd

P.P.M.	First Exposure	Animal No.	8-hour Exposures	Wt. in Grams	Weight Change During First 10 Exp.	Second 10 Exp.	Third 10 Exp.	30 Exp.
Control	8-20-40	R 8744	-	123	+ 50	+ 15	+ 23	+ 88
		R 8745	-	110	+ 55	+ 22	+ 24	+101
		R 8750	-	112	+ 48	+ 20	+ 43	+111
		R 8752	-	114	+ 39	+ 26	+ 13	+ 78
		Ave.			+ 48	+ 21	+ 26	+ 95
Control	8-20-40	P 8758	-	283	+124	- 3	- 32	+ 89
		P 8764	-	282	+125	+ 5	+ 16	+146
		P 8767	-	251	+ 67	+ 15	+ 11	+ 93
		P 8768	-	290	+115	+ 5	+ 32	+152
		P 8773	-	290	+ 86	+ 3	- 26	+ 63
		Ave.			+103	+ 5	+ 11	+119

Table 4-10S

Blood Counts on Animals Exposed Repeatedly to Isophorone Vapors

P.P.M.	Animal No.	Exposures	R.B.C. Millions	Hbg. Gm./ 100 ml.	W.B.C. Thousand	Poly.	Lymph.	Mono.	Eosin.	Baso.
500	R 2730 (died)	0	6.51	10.5	12.92	7	87	3	3	0
		2	7.69	12.2	8.56	14	81	3	2	0
		5	5.75	10.3	10.16	16	82	1	1	0
		9	8.30	9.5	10.44	17	75	2	6	0
		13	6.64	10.4	17.20	8	92	0	0	0
500	R 2732 (died)	0	6.78	10.0	11.20	13	83	3	1	0
		2	8.71	12.0	8.28	14	80	3	3	0
		5	5.93	10.4	7.48	20	76	0	4	0
		9	7.29	10.0	14.36	34	66	0	0	0
		13	7.46	10.6	20.76	4	91	5	0	0
		18	6.44	13.2	9.40	38	59	3	0	0
500	R 2733 (infected)	0	6.69	10.5	9.64	22	76	1	1	0
		2	6.43	12.4	9.36	14	83	0	3	0
		5	3.59	10.1	8.16	26	73	0	1	0
		9	6.10	12.6	7.56	11	85	1	3	0
		13	8.19	10.8	18.68	17	79	3	1	0
		18	4.31	8.3	9.32	38	60	2	0	0
		20	6.32	11.8	15.68	33	66	1	0	0
500	R 2731	0	6.64	9.7	10.64	20	79	0	1	0
		2	7.28	13.3	10.92	21	77	1	1	0
		5	6.59	10.0	10.04	6	92	0	2	0
		9	5.93	9.7	17.00	18	78	1	3	0
		13	6.93	8.7	25.56	6	92	2	0	0
		18	8.62	15.3	20.0	7	86	4	3	0
		20	7.38	12.4	13.60	31	67	2	0	0
		30	7.63	11.8	16.36	21	78	1	0	0
500	P 3403 (died)	0	5.66	11.0	6.36	25	71	0	4	0
		2	6.97	13.8	8.12	44	55	1	0	0
		5	5.94	11.0	7.48	16	82	0	2	0
		9	5.52	12.8	11.84	52	42	0	6	0
500	P 3405 (died)	0	5.74	10.5	4.12	38	62	0	0	0
		2	6.12	11.5	5.04	32	66	0	0	2
		5	6.05	11.6	11.60	40	59	1	0	0
		9	6.55	13.0	9.48	53	46	1	0	0

(Continued)

Table 4-108 Cont'd

P.P.M.	Animal No.	Expo-sures	R.B.C. Millions	Hbg. Gm./ 100 ml.	W.B.C. Thou-sand	Poly.	Lymph.	Mono.	Eosin.	Baso.
500	P 3404	0	5.11	10.5	5.00	17	80	1	0	2
		2	5.41	12.3	5.00	10	84	0	0	6
		5	5.11	10.0	9.64	42	58	0	0	0
		9	5.65	11.3	8.60	20	72	0	2	6
		13	5.47	12.0	18.28	72	26	1	0	1
		18	5.59	15.5	9.52	50	46	3	0	1
		20	7.19	15.0	10.48	37	62	0	0	1
		30	5.75	15.4	11.28	51	44	4	0	1
500	P 3406	0	6.16	10.6	3.40	14	85	1	0	0
		2	4.82	13.8	8.44	41	59	0	0	0
		5	4.36	11.2	10.28	25	75	0	0	0
		9	5.75	11.3	14.48	41	56	2	1	0
		13	6.34	9.9	10.34	36	64	0	0	0
		18	5.35	14.8	7.56	15	84	1	0	0
		20	5.82	15.1	18.40	69	31	0	0	0
		30	5.30	15.6	10.80	52	48	0	0	0
200	R 2933	0	6.84	14.3	8.64	15	84	1	0	0
		9	9.47	15.0	16.40	24	76	0	0	0
		22	9.32	18.5	18.04	8	90	2	0	0
		30	7.57	16.3	14.76	13	87	0	0	0
200	R 2934	0	6.84	15.0	13.64	7	90	1	2	0
		9	9.79	15.2	20.08	34	62	2	2	0
		22	6.86	15.8	14.36	25	74	1	0	0
		30	10.05	16.6	9.88	17	80	0	3	0
200	R 2935	0	7.13	13.2	11.88	18	71	2	9	0
		9	9.01	16.0	7.56	20	77	0	3	0
		22	8.40	16.3	10.04	17	81	1	1	0
		30	6.57	17.4	12.00	9	89	1	1	0
200	R 2936	0	7.75	17.6	10.12	6	92	2	0	0
		9	10.95	14.5	10.92	22	77	1	0	0
		22	8.68	16.3	11.28	34	64	2	0	0
		30	6.93	15.9	15.36	27	71	2	0	0
200	P 3743	0	5.41	13.1	4.64	34	62	2	0	2
	(died)	9	6.0	16.7	5.56	49	49	2	0	0
200	P 3742	0	6.60	15.6	5.76	30	65	5	0	0
		12	6.53	15.0	15.80	57	42	0	0	1
		20	4.34	14.8	17.04	62	36	1	0	1
		30	7.19	15.5	9.88	16	80	2	0	2

(Continued)

Table 4-106 Cont'd

P.P.M.	Animal No.	Exposures	R.B.C. Millions	Hbg. Gm./ 100 ml.	W.B.C. Thousand	Poly.	Lymph.	Mono.	Eosin.	Baso.
200	P 3745	0	7.57	13.0	3.12	54	45	0	1	0
		12	5.11	14.4	14.76	26	72	0	0	2
		20	6.00	13.7	14.76	59	40	0	1	0
		30	6.49	16.1	18.92	32	66	2	0	0
100	R 3172	0	6.54	15.3	10.28	18	82	0	0	0
		5	7.51	16.8	19.96	7	88	1	4	0
		14	6.03	17.0	17.88	13	85	0	2	0
		21	8.48	15.8	14.84	6	93	1	0	0
		30	9.18	18.9	13.20	9	91	0	0	0
100	R 3173	0	6.01	11.9	18.32	3	97	0	0	0
		5	6.92	14.0	12.00	17	82	1	0	0
		14	6.50	13.5	19.84	6	93	1	0	0
		21	10.84	16.0	12.92	12	84	2	2	0
		30	8.32	16.8	14.28	11	86	2	1	0
100	R 3174	0	6.02	12.5	19.44	18	82	0	0	0
		5	7.80	14.3	22.32	17	81	1	1	0
		14	7.13	15.0	14.76	14	81	3	2	0
		21	7.55	16.2	19.36	16	83	1	0	0
		30	9.62	18.0	18.72	22	75	0	3	0
100	R 3175	0	7.91	15.2	16.40	10	88	0	2	0
		5	8.86	15.3	11.52	15	83	1	1	0
		14	11.75	16.5	16.76	10	90	0	0	0
		21	8.56	15.5	13.48	22	77	0	1	0
		30	8.85	18.3	13.32	10	89	0	1	0
100	P 3831 (died, infected)	0	5.97	14.1	6.52	35	65	0	0	0
		5	4.99	13.9	10.76	11	83	0	1	5
		14	4.83	12.6	7.48	43	55	1	1	0
100	P 3829	0	5.56	13.4	6.04	31	65	3	0	1
		5	5.36	14.0	10.76	28	69	0	0	3
		14	5.75	13.9	15.48	55	42	2	1	0
		21	5.45	17.0	27.00	33	66	1	0	0
		30	6.32	18.0	16.52	27	71	1	0	1
100	P 3830	0	6.79	17.0	7.88	36	64	0	0	0
		5	5.10	14.6	18.48	20	74	2	0	4
		14	5.93	13.0	12.04	21	79	0	0	0
		21	6.10	14.8	10.32	49	50	0	1	0

(Continued)

Table 4-108 Cont'd

P.P.M.	Animal No.	Exposures	R.B.C. Millions	Hbg. Gm./ 100 ml.	W.B.C. Thousand	Poly.	Lymph.	Mono.	Eosin.	Baso.
100	P 3832	0	5.06	14.0	4.40	42	54	2	0	2
		5	5.68	14.7	23.16	72	26	2	0	0
		14	5.22	13.2	19.40	59	40	0	0	1
		21	5.42	11.5	9.76	56	42	2	0	0
		30	7.16	16.8	5.12	24	72	4	0	0
50	R 3643	0	8.92	15.0	8.04	14	80	2	4	0
	(died,	7	7.43	15.0	9.12	10	88	1	1	0
	infected)	17	10.39	18.0	5.00	10	85	0	5	0
50	R 3640	0	6.60	14.3	9.96	11	84	3	2	0
		7	6.95	15.8	16.12	23	75	1	1	0
		17	5.94	18.3	17.52	19	79	2	0	0
		27	8.00	15.2	12.40	21	77	2	0	0
50	R 3641	0	7.15	13.9	10.60	21	77	0	2	0
		7	6.66	15.2	15.32	14	82	2	2	0
		17	7.38	15.7	11.88	25	72	0	3	0
		27	8.17	14.6	10.40	9	91	0	0	0
50	R 3642	0	7.65	13.4	17.08	16	82	2	0	0
		7	5.73	12.6	20.76	10	88	1	1	0
		17	8.17	15.9	16.76	38	61	1	0	0
		27	6.67	14.8	11.52	14	84	1	1	0
25	R 8733	0	6.28	13.2	17.12	9	79	9	2	1
		30	8.10	14.6	8.44	9	88	3	0	0
25	R 8735	0	8.16	12.4	10.24	37	58	5	0	0
		30	7.88	14.0	8.12	22	71	5	2	0
25	R 8739	0	6.79	11.8	11.56	10	80	10	0	0
		30	7.13	13.6	12.28	12	84	3	1	0
25	R 8740	0	6.73	12.0	12.12	36	61	3	0	0
		30	6.74	14.4	9.20	19	79	2	0	0
25	P 8755	0	6.18	14.2	4.56	15	76	5	4	0
		30	7.26	14.4	4.92	21	68	9	0	2
25	P 8761	0	5.76	12.4	7.84	27	69	4	0	0
		30	5.50	11.6	5.00	4	88	7	0	1

(Continued)

Table 4-108 Cont'd

P.P.M.	Animal No.	Exposures	R.B.C. Millions	Hbg. Gm./ 100 ml.	W.B.C. Thousand	Poly.	Lymph.	Mono.	Eosin.	Baso.
25	P 8763	0	5.91	13.0	4.80	6	90	4	0	0
		30	4.96	13.2	9.76	19	74	7	0	0
25	P 8772	0	6.71	13.0	10.68	7	86	5	2	0
		30	5.79	11.6	6.00	10	71	7	2	0
Control	R 8744	0	7.19	10.8	19.76	39	59	0	2	0
		30	9.08	15.2	6.04	10	78	12	0	0
Control	R 8745	0	6.12	11.0	8.04	31	63	4	2	0
		30	6.62	14.4	10.12	16	76	2	6	0
Control	R 8750	0	6.84	10.8	10.52	13	77	3	7	0
		30	9.00	15.2	7.40	8	90	2	0	0
Control	R 8752	0	6.12	10.6	14.56	13	75	12	0	0
		30	8.30	15.2	10.45	11	71	15	2	1
Control	P 8764	0	5.88	11.4	6.12	59	28	11	0	2
		30	3.12	11.2	6.96	36	61	2	1	0
Control	P 8767	0	5.42	12.0	6.40	70	25	5	0	0
		30	5.14	13.0	5.60	6	84	8	2	0
Control	P 8773	0	6.77	13.4	6.68	10	70	18	2	0
		30	5.21	14.0	5.44	56	35	7	0	2

Table 4-109

Micropathology from Repeated Exposures to Isophorone Vapors

See key to abbreviations following table

P.P.M.	Species	Animal No.	8-Hour Exposures	Fate	Accident or Infection	Micropathology
500	Rat	R 2736	7	D	-	H, Kcdt, Lcw, LUcrs, Sc
		R 2735	10	D	-	H, Kcdt, LCknW, LUCer, Scs
		R 2734	16	D	-	H, Kbcdw, LcW, LUC, Sc
		R 2730	17	D	-	H, KCdTw, LCw, LUCr, SC
		R 2732	21	D	-	-
		R 2739	10	S	-	H, Knt, Sc
		R 2737	20	S	LUp	H, K, L, LUcx, Sc
		R 2738	20	S	-	H, K, L, LUc, S
		R 2733	24	S	M, CPn	Hist, Kbcdw, Lcw, LUcp, Sc
		R 2731	30	S	-	H, K, L, LU, S
	G. Pig	P 3403	10	D	-	H, KcnW, Lcw, LUCprs, S
		P 3405	10	D	-	H, Kbcw, Lw, LUbcp, Scn
		P 3410	12	D	-	H, KcnW, Lcw, LUcrs, S
		P 3411	16	D	-	H, KcNW, Lcnw, LUCrs, S
		P 3412	10	S	-	H, Kbcsw, Lw, LUCrs, S
		P 3408	20	S	-	H, Kbdsw, L, LUcs, S
		P 3409	20	S	-	H, Kbdsw, L, LUcs, S
		P 3404	30	S	-	H, K, L, LUc, S
		P 3406	30	S	-	H, Kbdsw, L, LUCfrs, S
		P 3407	30	S	-	H, Kw, L, S
200	Rat	R 2940	20	D	-	H, Kdw, L, LUCbrs, Sc
		R 2937	10	S	-	-
		R 2933	30	S	-	H, Ks, L, LUr, S
		R 2934	30	S	-	-
		R 2935	30	S	-	H, Kcntw, LUcr, Sc
		R 2936	30	S	-	H, Kcntw, LUcr, Sc
		R 2938	30	S	-	-
		R 2939	30	S	-	-
		R 2941	30	S	-	-
		R 2942	30	S	-	H, K, L, LUc, S
	G. Pig	P 3834	5	D	LUi	-
		P 3836	10	D	-	-
		P 3743	11	D	-	-
		P 3837	10	S	-	-
		P 3838	10	S	-	-
		P 3833	20	S	-	H, Kw, L, LUac, S
		P 3835	20	S	-	H, K, L, LUbcr, S
		P 3742	30	S	-	-
		P 3745	30	S	-	H, K, L, LUc, S

(Continued)

Table 4-109 Cont'd

P.P.M.	Species	Animal No.	8-Hour Exposures	Fate	Accident or Infection	Micropathology
100	Rat	R 3180	10	D	-	-
		R 3181	10	D	-	H, KcTw, L, LUcr, Sc
		R 3176	20	S	-	-
		R 3177	20	S	-	-
		R 3172	30	S	-	H, Ktw, L, LUcr, Sc
		R 3173	30	S	-	H, Ktw, L, LUcs, Sc
		R 3174	30	S	-	H, Kctw, L, LUcs, Sc
		R 3175	30	S	-	H, Kctw, L, LUcr, Sc
		R 3178	30	S	-	-
		R 3179	30	S	-	H, K, L, LUc, S
	G. Pig	P 3839	8	D	IP	-
		P 3831	21	D	IP	Hv, KsWX, Lw, LUc
		P 3842	10	S	-	-
		P 3843	10	S	-	-
		P 3840	20	S	-	H, Kw, LUcrs, S
		P 3841	20	S	-	H, Kw, L, LUcep, S
		P 3829	30	S	-	-
		P 3830	30	S	-	-
		P 3832	30	S	-	H, K, L, S
50	Rat	R 3800	1	D	IP	-
		R 3643	22	D	LP	H, Kodw, Lepw, LUcr, Scs
		R 3644	10	S	-	-
		R 3802	10	S	-	-
		R 3801	20	S	-	H, K, Lw, LUces, S
		R 3798	20	S	-	H, Kt, L, LUc, S
		R 3799	20	S	-	H, Kw, L, LUs, S
		R 3640	30	S	-	H, Kg, L, LUcs, S
		R 3641	30	S	-	H, K, L, LUcs, S
		R 3642	30	S	-	H, Kb, L, LU, S
25	Rat	R 8733	30	S	-	K, L, LUc
		R 8734	30	S	-	K, L, LUC
		R 8735	30	S	-	K, L, LUC
		R 8737	30	S	-	K, L, LUC
		R 8738	30	S	-	K, L, LUc
		R 8739	30	S	-	-
		R 8740	30	S	-	-
		R 8741	30	S	-	-
		R 8747	30	S	-	-
		R 8748	30	S	-	-

(Continued)

Key to Abbreviations in Table 4-109

Column	Symbol	Meaning
Fate	D	Died
	S	Sacrificed for examination
Infection	CPn	Catarrhal pneumonia
	IP	Intestinal parasites
	LP	Liver parasites
	LUi	Lung infection
	LUp	Lung parasite
	M	Myocarditis
	TB	Tuberculosis
Micropathology		(Initial capital for organ, followed by small letters for slight or capitals for marked effects)
	H	Heart, normal
	Hi	" , round cell infiltration
	Hm	" , myocarditis
	Ht	" , connective tissue infiltration
	Hv	" , coronary vessels dilated
	K	Kidney, normal
	Kb	" , increased fluid in Bowman's capsule
	Kc	" , congested
	Kd	" , toxic degeneration of convoluted tubules
	Kg	" , granular detritis in convoluted tubules
	Kn	" , necrosis of tubular epithelium
	Ks	" , frothy secretion in convoluted tubules
	Kt	" , granular secretion in convoluted tubules
	Kw	" , cloudy swelling of convoluted tubules
	Kx	" , cloudy swelling of loop tubules
	L	Liver, normal
	Lc	" , congested
	Lh	" , hemorrhages
	Lk	" , Kupfer cells prominent
	Ln	" , necrosis
	Lp	" , parasites
	Lw	" , cloudy swelling
	LU	Lung, normal
	LUa	" , subpleural consolidation
	LUb	" , red cells in bronchioles
	LUc	", congestion
	LUd	", desquamation of alveolar epithelium
	LUe	" , desquamation of bronchial epithelium
	LUf	" , fibrin in alveoli
	LUp	" , pneumonia
	LUr	" , red cells in alveoli
	LUs	" , increased secretion in bronchioles

(continued)

Table 4-109 Cont'd

Column	Symbol	Meaning
	LUt	Lung, tuberculosis
	LUx	" , parasites
	S	Spleen, normal
	Se	" , congested
	Sp	" , phagocysed pigment
	Ss	" , splenocytes prominent

CERTIFICATE OF AUTHENTICITY

THIS IS TO CERTIFY that the microimages appearing on this microfiche are accurate and complete reproductions of the records of U.S. Environmental Protection Agency documents as delivered in the regular course of business for microfilming.

Data produced 1 16 93 Marcia Tubolino
(Month) (Day) (Year) Camera Operator

Place Syracuse New York
(City) (State)

AMTEK
corp